DAA treatment among people who use or inject drugs: a systematic review and meta-analysis

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Disclosure

None to disclose

Introduction

- People who inject drugs are a priority population for scale-up of HCV testing, linkage to care, and treatment, given the high burden of HCV in this population.

  Grebely et al. Addiction 2018

- There are restrictions for the reimbursement of DAA therapy for people with ongoing drug use in some states in the USA and Europe.

  Marshall et al. Lancet Gastroenterol Hepatol 2018; Barua et al. Ann Int Med 2015

- Among clinicians attending the Liver Meeting® in 2014, 15% were willing to treat an individuals who recently injected drugs using DAA regimens. Reinfection and adherence to treatment were reported as their most important concerns
  - *Asher et al. Subst Use Misuse 2016*

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Objectives

- To evaluate DAA treatment completion, sustained virological response (SVR), and loss to follow-up among overlapping populations of:
  - people with recent drug use (injecting or noninjecting),
  - people with recent injecting drug use,
  - people receiving opioid substitution therapy (OST).
- To assess the factors explaining heterogeneity across studies.

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Methods – Eligibility criteria

- Studies investigating DAA treatment outcome among people with HCV infection, if they met all the following criteria:

  a) Study population included defined populations of people with recent drug use or people receiving OST

  b) Treatment included interferon-free DAA regimens

  c) Both treatment completion and SVR were reported.

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Methods – Information sources

- Bibliographic databases:
  - MEDLINE (Pubmed)
  - Scopus
  - Web of Science
  - Cochrane Central Register of Controlled Trials (CENTRAL)
  - PsycINFO

- Conference presentations:
  - International Liver Congress™
  - The Liver Meeting®
  - Annual Conference on Retroviruses and Opportunistic Infections (CROI)
  - International Symposium on Hepatitis Care in Substance Users (INHSU)

- ClinicalTrials.gov was searched for registered clinical trials, including ongoing studies.

- Searches were performed in Dec 2017, and updated in Mar 2018.

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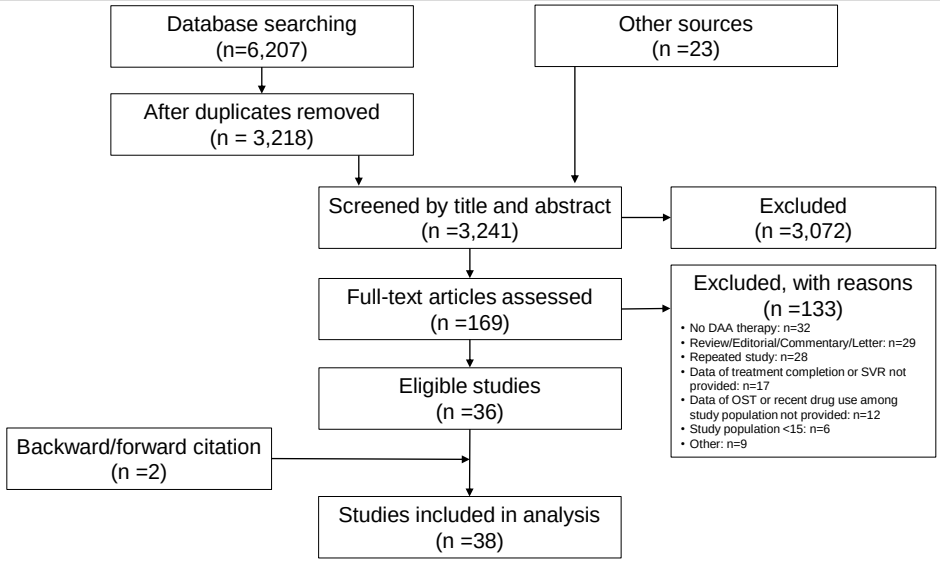
Results



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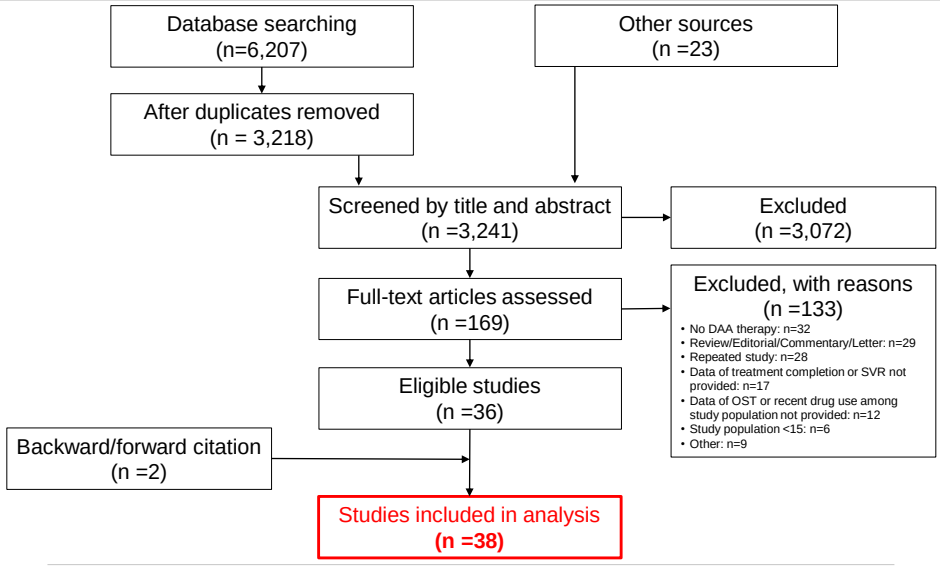
Results



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Results

	Study n (%)
Study design	
Observational	28 (74%)
Clinical trial	10 (26%)
Study setting	
Community clinic	3 (8%)
Drug treatment service	11 (29%)
Primary care	3 (8%)
Tertiary care	5 (13%)
Mixed	13 (34%)
Other/Not reported	3 (8%)
Definition of "recent drug use"	
During the past 1 or 3 months	7 (19%)
During the past 6 or 12 months	12 (31%)
At initiation or during DAA therapy	9 (24%)
Ongoing or active drug use	3 (8%)
Combination of two definitions	4 (11%)
Not reported	3 (8%)

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Results

Overlapping study population or sub-population

	Study n	Participant n	Participant n in each study, range
Total	**38**	**3,634**	**16 - 472**
Recent drug use (with or without OST)	21	1,408	9 – 235
OST (with or without recent drug use)	36	2,987	16 - 472

Exclusive study population or sub-population

	Study n	Participant n	Participant n in each study, range
Recent IDU (with or without OST)	8	670	18 - 163
OST (with or without recent drug use)	25	2,331	14 – 472
Other	10	633	21 – 137
Total	**45**	**3,634**	

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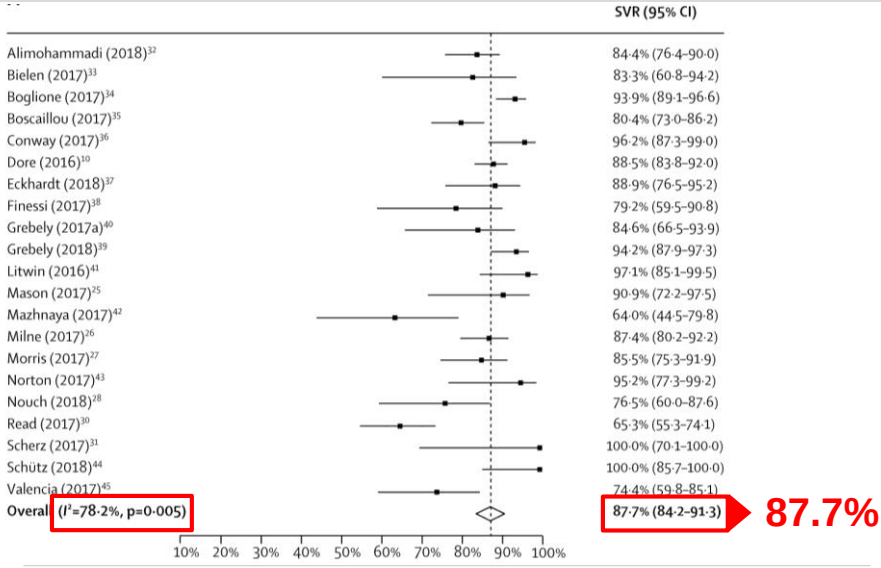
Results – ITT SVR, individuals with recent drug use



87.7%

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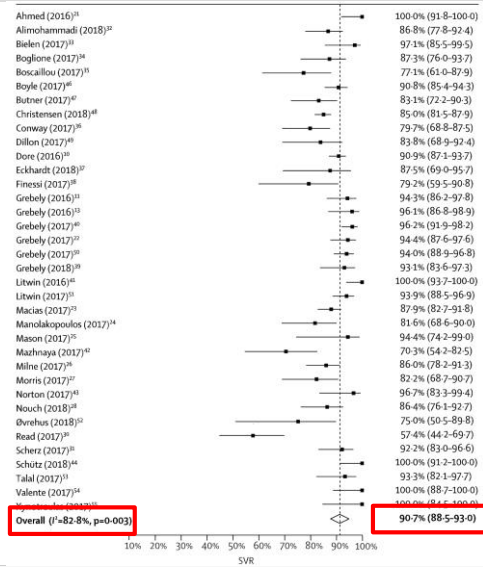
Results – ITT SVR, individuals on OST



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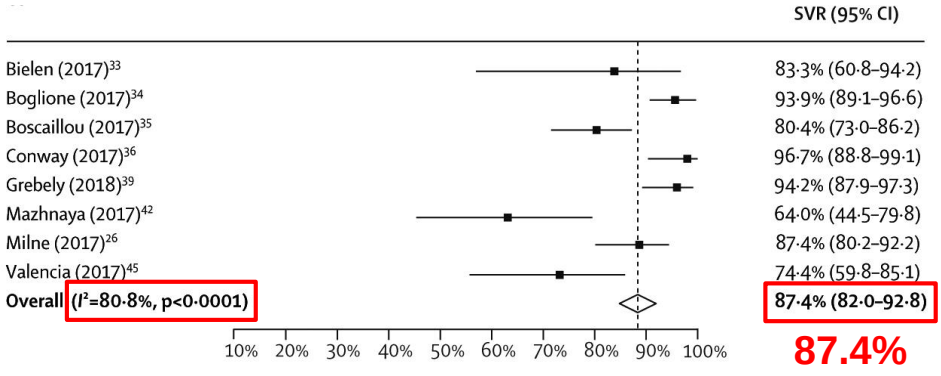
Results – ITT SVR, individuals with recent IDU



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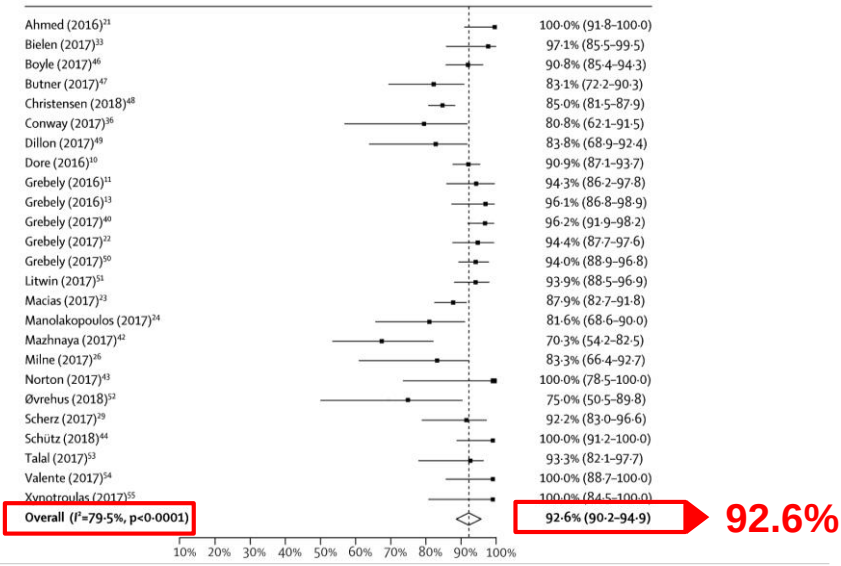
Results – ITT SVR, individuals on OST



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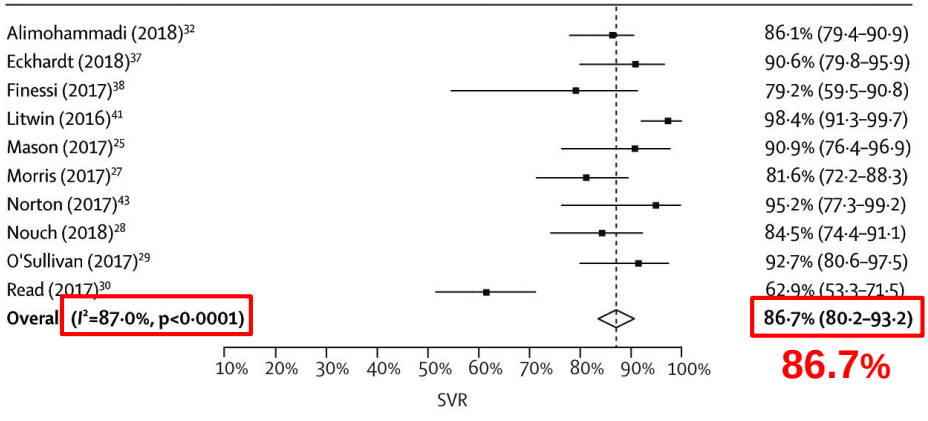
Results – ITT SVR, other study population



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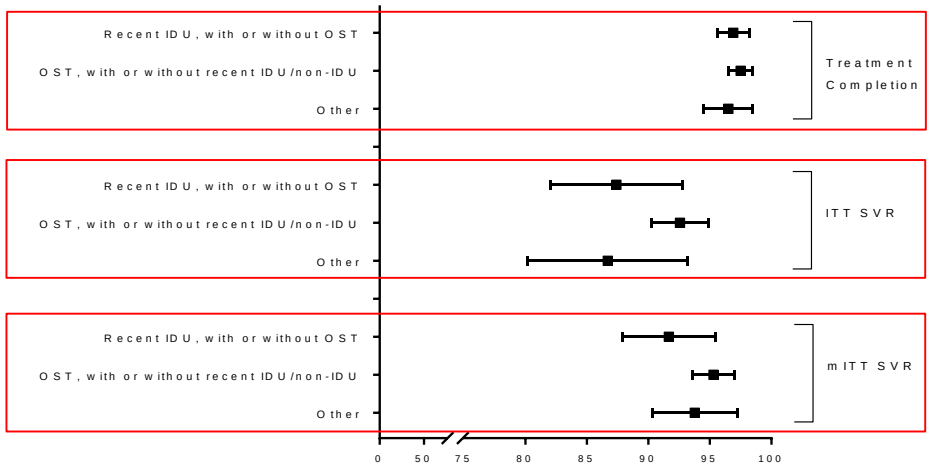
Results – Study population



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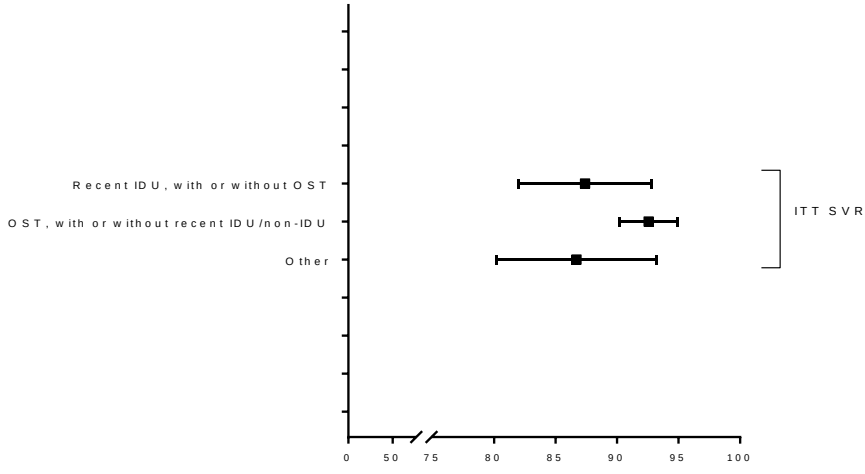
Results – Study population



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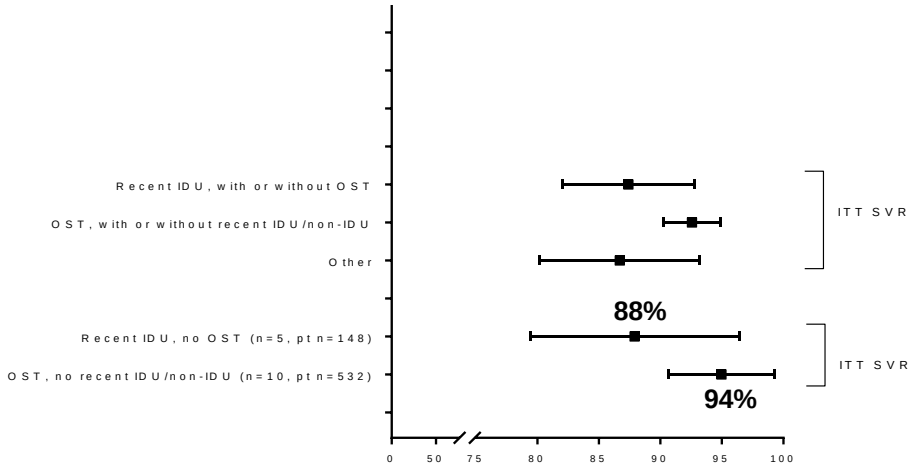
Results – Study population



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Results – Meta-regression, IT SVR

	Unadjusted models OR (95% CI)	P
Proportion of participants with recent drug use	0.95 (0.89-1.02)	0.171
Proportion of participants receiving OST	1.08 (0.99-1.19)	0.066
Proportion of men	0.78 (0.59-1.03)	0.084
Median/mean age	1.06 (1.01, 1.12)	0.013
Proportion of participants with cirrhosis	1.00 (0.87-1.14)	0.997
Proportion of treatment experienced participants	1.10 (0.90-1.35)	0.324
Proportion of participants with HIV co-infection	0.87 (0.77-0.98)	0.021
Study design		
Observational	1.00	
Clinical Trial	2.09 (1.23-3.57)	0.008
Study population		
Recent IDU, with or without OST	1.00	
OST, with or without recent IDU/non-IDU	1.47 (0.76-2.84)	0.250
Other	0.96 (0.44-2.09)	0.924

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Results – Meta-regression, ITT SVR

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Results – Meta-regression, ITT SVR

	Adjusted model OR (95% CI)	P
Participants with recent drug use		
Participants receiving OST	1.04 (0.96-1.12)	0.364
Men	1.07 (0.82-1.39)	0.612
Median/mean age	1.07 (1.02-1.12)	0.008
Participants with HIV co-infection	0.96 (0.86-1.07)	0.427
Study design		
Observational	1.00	
Clinical Trial	2.18 (1.27-3.75)	0.006

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Results – Meta-regression

ITT SVR

	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Study design				
Observational	1.00		1.00	
Clinical Trial	2.09 (1.23-3.57)	0.008	2.18 (1.27-3.75)	0.006
Treatment completion				
Observational	1.00		1.00	
Clinical Trial	1.90 (1.20-3.01)	0.018	1.45 (0.87-2.43)	0.148
Loss to follow-up				
Observational	1.00		1.00	
Clinical Trial	0.45 (0.22-0.93)	0.032	0.45 (0.22-0.94)	0.033
mITT SVR				
Observational	1.00		1.00	
Clinical Trial	1.86 (1.15-3.05)	0.013	1.36 (0.73-2.56)	0.323

Limitation

- Given the relatively recent availability of DAA treatment, it is possible that the study populations were those who were more motivated to receive treatment and therefore less representative of people with recent drug use in general.
- Definitions for recent drug use varied across studies.
- Several studies conducted interventions to enhance adherence, such as directly observed therapy, group treatment, and nurse or peer support. The effect of these interventions on treatment outcome was not assessed in this study given the wide heterogeneity among interventions.
- We did not include the study setting in meta-regression analysis given that most studies, particularly multi-centre studies, had been conducted in more than one setting, and could not be assigned to a single study setting category.

Conclusion

- This study showed favourable DAA treatment outcome among people with recent drug use and those receiving opioid substitution therapy.
- Lower SVR was observed among people who have recently used drugs (both injecting and non-injecting), with post-treatment loss to follow-up primarily contributing to the decreased SVR in this population.
- Clinical trials had higher SVR and lower loss to follow-up, compared to observational studies.
- Collectively, this study provides robust evidence to inform clinical and public health management of HCV infection among people who inject drugs.

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